hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

E' Cont

2. (**Twice Amended**) A method for treatment or prophylaxis of toxin-induced peripheral neuropathy, comprising systemically administering to the patient an amount of a *hedgehog* polypeptide modified with two or more lipophilic moieties effective to treat or prophylactically treat toxin-induced peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

E2

3. (**Thrice Amended**) A method for the treatment or prophylaxis of peripheral neuropathy comprising systemically administering to an animal an amount of a *hedgehog* polypeptide modified with two or more lipophilic moieties sufficient to treat or prophylactically treat peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

4. (**Thrice Amended**) A method for protecting peripheral nerve cells under conditions which otherwise result in peripheral neuropathy, comprising systemically administering to a patient in need thereof an effective amount of a *hedgehog* polypeptide modified with two or more lipophilic moieties sufficient to protect peripheral nerve cells from peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally

occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

E2 cont.

5. (**Twice Amended**) A method for the treatment or prophylaxis of diabetic neuropathy comprising systemically administering to a patient in need thereof an effective amount of a *hedgehog* polypeptide modified with two or more lipophilic moieties sufficient to treat or prophylactically treat diabetic neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

E3

6. (**Twice Amended**) A method for the treatment or prophylaxis of virally induced peripheral neuropathy comprising systemically administering to a patient in need thereof an effective amount of a *hedgehog* polypeptide modified with two or more lipophilic moieties sufficient to treat or prophylactically treat virally induced peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

E4

9. (**Twice Amended**) The method of any of claims 1-6, wherein the *hedgehog* amino acid sequence is at least 90 percent identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues.

10. (**Twice Amended**) The method of claim 9, wherein the *hedgehog* amino acid sequence is encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to at least one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6.

E4 cont.

11. (**Twice Amended**) The method of claim 9, wherein the *hedgehog* amino acid sequence is a vertebrate *hedgehog* polypeptide.

E5

13. (**Twice Amended**) The method of claim 9, wherein the polypeptide includes at least a 50 amino acid extracellular portion of a vertebrate *hedgehog* polypeptide selected from at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15.

14. (**Twice Amended**) The method of claim 9, wherein the polypeptide includes at least a 150 amino acid extracellular portion of a vertebrate *hedgehog* polypeptide selected from at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15.

15. (**Twice Amended**) The method of claim 9, wherein the polypeptide includes at least an extracellular portion of a vertebrate *hedgehog* polypeptide corresponding to residues 24-194 of SEQ ID No:15.

16. (**Twice Amended**) The method of claim 9, wherein the polypeptide is modified with two or more lipophilic moieties.

17. (**Reiterated**) The method of claim 16, wherein the polypeptide is modified with one or more sterol moieties.

18. (**Reiterated**) The method of claim 17, wherein the sterol moiety is cholesterol.

19. (**Reiterated**) The method of claim 16, wherein the polypeptide is modified with one or more fatty acid moieties.

20. (**Reiterated**) The method of claim 19, wherein each fatty acid moiety is independently selected from myristoyl, palmitoyl, stearoyl, or arachidoyl.

21. (**Reiterated**) The method of claim 16, wherein the polypeptide is modified with one or more aromatic hydrocarbons.

22. (**Reiterated**) The method of claim 21, wherein each aromatic hydrocarbon is independently selected from benzene, perylene, phenanthrene, anthracene, naphthalene, pyrene, chrysene, or naphthacene.

23. (**Reiterated**) The method of claim 16, wherein the polypeptide is modified one or more times with a C7 - C30 alkyl or cycloalkyl.

30. (**Reiterated**) The method of any of claims 1-6, wherein the *hedgehog* agonist mimics *hedgehog* signal transduction by altering the localization, protein-protein binding and/or enzymatic activity of an intracellular protein involved in *hedgehog* signaling.

31. (**Reiterated**) The method of any of claims 1-6, wherein the *hedgehog* agonist alters the level of expression of a *hedgehog* protein, a *patched* protein or a protein involved in *hedgehog* signal transduction.

41. (**Reiterated**) The method of any of claims 4-6, wherein the patient is being treated prophylactically.

44. (**Reiterated**) The method of claim 4, 5, or 6, which method is part of a protocol for the treatment of an acquired neuropathy.

45. (**Reiterated**) The method of claim 44, wherein the neuropathy is due to viral infection, diabetes or inflammation.

46. (**Reiterated**) The method of claim 44, wherein the neuropathy is due to contact with a toxic agent.

47. (**Reiterated**) The method of claim 44, wherein the neuropathy is selected from diabetic neuropathy; immune-mediated neuropathy, chronic inflammatory demyelinating polyneuropathy (CIDP), chronic polyneuropathy with antibodies to peripheral nerves, neuropathies associated with vasculitis or inflammation of the blood vessels in peripheral nerve, brachial or lumbosacral plexitis, and neuropathies associated with monoclonal gammopathies; neuropathies associated with tumors or neoplasms such as sensory neuropathy associated with lung cancer, neuropathy associated with multiple myeloma, neuropathy associated with waldenstrom's macroglobulemia, chronic lymphocytic leukemia, or B-cell lymphoma; neuropathy associated with amyloidosis; neuropathies caused by infections; neuropathies caused by nutritional imbalance; neuropathy in kidney disease; hypothyroid neuropathy; neuropathy caused by alcohol and toxins; neuropathies caused by drugs; neuropathy resulting from local irradiation; neuropathies caused by trauma or compression; or idiopathic neuropathies.

48. (**Reiterated**) The method of claim 4, 5, or 6, which method is part of a protocol for the treatment of a hereditary neuropathy.

50. (**Reiterated**) The method of claim 4, 5, or 6, which method is part of a protocol for slowing neurodegenerative events associated with age-related neuropathology.

E6 51. (**Twice Amended**) The method of claim 9, wherein the polypeptide is a fusion protein.

E7 52. (**Amended**) The method of claim 9, wherein the *hedgehog* amino acid sequence is at least 95 percent identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues.

53. (**Amended**) The method of claim 9, wherein the *hedgehog* amino acid sequence is identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues.

E8 55. (**Amended**) The method of claim 9, wherein the N-terminal fragments have a molecular weight of about 19 kD.

Please add the following new claims:

59. (**New**) A method for treatment or prophylaxis of toxin-induced peripheral neuropathy, comprising systemically administering to a patient an amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective to treat or prophylactically treat toxin-induced peripheral neuropathy, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to one or more internal amino acid residues.

60. (**New**) A method for treatment or prophylaxis of peripheral neuropathy comprising systemically administering to an animal an amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective for the treatment or prophylaxis of peripheral neuropathy, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to one or more internal amino acid residues.

61. (**New**) A method for protecting peripheral nerve cells under conditions which otherwise result in peripheral neuropathy, comprising systemically administering to a patient in need thereof an amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective for protecting peripheral nerve cells, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to one or more internal amino acid residues.

62. (**New**) A method for treatment or prophylaxis of diabetic neuropathy comprising systemically administering to a patient in need thereof an amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective for the treatment or prophylaxis of diabetic neuropathy, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to one or more internal amino acid residues.

E9 cont.

63. (**New**) A method for treatment or prophylaxis of virally induced peripheral neuropathy comprising systemically administering to a patient in need thereof an amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective for the treatment or prophylaxis of virally induced peripheral neuropathy, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to one or more internal amino acid residues.

64. (**New**) A method for treatment or prophylaxis of toxin-induced peripheral neuropathy, comprising systemically administering to a patient an amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective to inhibit dysfunction of motor or sensory nerve cells, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to one or more internal amino acid residues.

65. (**New**) A method for treatment or prophylaxis of peripheral neuropathy comprising systemically administering to an animal an amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective for the treatment or prophylaxis of peripheral neuropathy, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to one or more internal amino acid residues.

E9 cont.

66. (**New**) A method for protecting peripheral nerve cells under conditions which otherwise result in peripheral neuropathy, comprising systemically administering to a patient in need thereof an amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective for protecting peripheral nerve cells, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to one or more internal amino acid residues.

67. (**New**) A method for treatment or prophylaxis of diabetic neuropathy comprising systemically administering to a patient in need thereof an amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective for the treatment or prophylaxis of diabetic neuropathy, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to one or more internal amino acid residues.

68. (**New**) A method for treatment or prophylaxis of virally induced peripheral neuropathy comprising systemically administering to a patient in need thereof amount of a *hedgehog* polypeptide modified with one or more lipophilic moieties effective for the treatment or prophylaxis of virally induced peripheral neuropathy, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said lipophilic modification comprises addition of one or more lipophilic moieties to one or more internal amino acid residues.

E9 cont.

69. (**New**) A method for treatment or prophylaxis of toxin-induced peripheral neuropathy, comprising systemically administering to a patient an amount of a *hedgehog* polypeptide modified with two or more lipophilic moieties effective to inhibit dysfunction of motor or sensory nerve cells, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

70. (**New**) A method for treatment or prophylaxis of peripheral neuropathy comprising systemically administering to an animal an amount of a *hedgehog* polypeptide modified with two or more lipophilic moieties effective for the treatment or prophylaxis of peripheral neuropathy, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

71. (**New**) A method for protecting peripheral nerve cells under conditions which otherwise result in peripheral neuropathy, comprising systemically administering to a patient in need thereof an amount of a *hedgehog* polypeptide modified with two or more lipophilic moieties effective for protecting peripheral nerve cells, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

E9 Cont.

72. (**New**) A method for treatment or prophylaxis of diabetic neuropathy comprising systemically administering to a patient in need thereof an amount of a *hedgehog* polypeptide modified with two or more lipophilic moieties effective for the treatment or prophylaxis of diabetic neuropathy, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

73. (**New**) A method for treatment or prophylaxis of virally induced peripheral neuropathy comprising systemically administering to a patient in need thereof amount of a *hedgehog* polypeptide modified with two or more lipophilic moieties effective for the treatment or prophylaxis of virally induced peripheral neuropathy, wherein the *hedgehog* polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residues.

The amended claims are re-stated below to reflect changes with respect to the last filing.

1. **(Twice Amended)** A method for inhibiting degradation in functional performance of motor or sensory nerves in an animal, comprising systemically administering to the animal an amount of a *hedgehog* ~~agonist~~ polypeptide modified with two or more lipophilic moieties sufficient to inhibit degradation in the functional performance of motor or sensory nerves, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

2. **(Twice Amended)** A method for treatment or prophylaxis of toxin-induced peripheral neuropathy, ~~inhibiting dysfunction of motor or sensory nerve cells in a patient~~ comprising systemically administering to the patient an amount of a *hedgehog* ~~agonist~~ polypeptide modified with two or more lipophilic moieties effective to ~~inhibit dysfunction of motor or sensory nerve cells~~ treat or prophylactically treat toxin-induced peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

3. **(Thrice Amended)** A method for the treatment or prophylaxis of peripheral neuropathy comprising systemically administering to an animal an amount of a *hedgehog* ~~agonist~~ polypeptide modified with two or more lipophilic moieties sufficient to treat or prophylactically treat peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13,

SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

4. (**Thrice Amended**) A method for protecting peripheral nerve cells under conditions which otherwise result in peripheral neuropathy, comprising systemically administering to a patient in need thereof an effective amount of a *hedgehog* ~~agonist~~ polypeptide modified with two or more lipophilic moieties sufficient to protect peripheral nerve cells from peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

5. (**Twice Amended**) A method for the treatment or prophylaxis of diabetic neuropathy comprising systemically administering to a patient in need thereof an effective amount of a *hedgehog* ~~agonist~~ polypeptide modified with two or more lipophilic moieties sufficient to treat or prophylactically treat diabetic neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

6. (**Twice Amended**) A method for the treatment or prophylaxis of virally induced peripheral neuropathy comprising systemically administering to a patient in need thereof an effective amount of a *hedgehog* ~~agonist~~ polypeptide modified with two or more lipophilic moieties sufficient to treat or prophylactically treat virally induced peripheral neuropathy, wherein the hedgehog polypeptide comprises an amino acid sequence that a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and b) is at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15,

or an N-terminal fragment thereof of at least 50 contiguous amino acid residues, and wherein said lipophilic modification comprises addition of two or more lipophilic moieties to an N-terminal amino acid residue.

9. (**Twice Amended**) The method of any of claims 1-6 ~~claim 7~~, wherein the *hedgehog* amino acid sequence is at least 90 percent identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15, or an N-terminal fragment thereof of at least 50 contiguous amino acid residues ~~SEQ ID Nos. 10-18 or any fragment thereof that binds to a *patched* polypeptide~~.

10. (**Twice Amended**) The method of claim 9 ~~7~~, wherein the *hedgehog* amino acid sequence is encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to at least one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6 ~~SEQ ID Nos. 1-9~~.

11. (**Twice Amended**) The method of claim 9 ~~7~~, wherein the *hedgehog* amino acid sequence is a vertebrate *hedgehog* polypeptide.

13. (**Twice Amended**) The method of claim 9 ~~7~~, wherein the polypeptide includes at least a 50 amino acid extracellular portion of a vertebrate *hedgehog* polypeptide selected from at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15 ~~SEQ ID Nos. 10-18~~.

14. (**Twice Amended**) The method of claim 9 ~~7~~, wherein the polypeptide includes at least a 150 amino acid extracellular portion of a vertebrate *hedgehog* polypeptide selected from at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID No: 15 ~~SEQ ID Nos. 10-18~~.

15. (**Twice Amended**) The method of claim 9 ~~7~~, wherein the polypeptide includes at least an extracellular portion of a vertebrate *hedgehog* polypeptide corresponding to residues 24-194 of SEQ ID No:15.